

## CLAIM AMENDMENTS

Claim 1 (currently amended)      A method of reducing nephrotoxicity in an individual during radioimmunotherapeutic treatment of a pathophysiological condition, comprising:

administering a pharmacologically effective dose of at least one adjuvant, wherein said adjuvant is a chelator, a diuretic, a competitive metal blocker, or a combination thereof, effective for preventing accumulation of a ~~metal~~ alpha-particle emitting daughters of actinium-225 radioisotope in kidneys

administering an actinium-225 radioimmunoconjugate to treat the pathophysiological condition;and

preventing accumulation of said alpha particle-emitting daughters of said actinium-225 within the kidneys of the individual via interaction between said adjuvant and said <sup>225</sup>Ac daughters or the kidney tissue or a combination thereof thereby reducing nephrotoxicity during the radioimmunotherapeutic treatment.

Claim 2 (original).    The method of claim 1, wherein said adjuvant(s) is administered prior to administering said actinium-225 radioimmunoconjugate, said adjuvant(s) continuing to be administered after said actinium-225 radioimmunoconjugate.

Claim 3 (canceled)    The method of claim 1, wherein said adjuvant is a chelator, a diuretic, a competitive metal blocker, or a combination thereof.

Claim 4 (currently amended)      The method of claim 3, 1, wherein said chelator is a dithiol chelating agent, 2,3 dimercapto-1-propane sulfonic acid, meso 2,3-dimercapto succinic acid, or a diethylenetriamine pentaacetic acid, calcium diethylenetriamine pentaacetic acid, or zinc diethylenetriamine pentaacetic acid.

Claim 5 (original) The method of claim 3, 1, wherein said diuretic is furosemide, chlorthiazide, hydrochlorothiazide, bumex or other loop diuretic.

Claim 6 (currently amended) The method of claim 3 1, wherein said competitive metal blocker is bismuth subnitrate or bismuth subcitrate.

Claim 7 (original) The method of claim 1, wherein said <sup>225</sup>Ac daughter is bismuth-213, francium-221 or a combination thereof.

Claim 8 (original) The method of claim 1, wherein said actinium-225 radioimmunoconjugate comprises an actinium-225 bifunctional chelant and a monoclonal antibody.

Claim 9 (original) The method of claim 8, wherein said actinium-225 radioimmunoconjugate is [<sup>225</sup>Ac] DOTA-HuM195.

Claim 10 (original) The method of claim 1, wherein said pathophysiological condition is a cancer or an autoimmune disorder.

Claim 11 (original) The method of claim 1, wherein said cancer is a solid cancer, a disseminated cancer or a micrometastatic cancer.

Claim 12 (original) The method of claim 11, wherein said cancer is myeloid leukemia.

Claim 13 (original) A method of reducing nephrotoxicity in an individual during radioimmunotherapeutic treatment a pathophysiological condition, comprising:

administering a pharmacologically effective dose of a chelator;  
administering an actinium-225 radioimmunoconjugate to treat the cancer; and

preventing accumulation of bismuth-213 daughters of said actinium-225 within the kidneys of the individual by scavenging thereof with said chelator thereby reducing nephrotoxicity during the radioimmunotherapeutic treatment.

Claim 14 (original) The method of claim 13, wherein said chelator is administered prior to administering said  $^{225}\text{Ac}$  radioimmunoconjugate, said chelator continuing to be administered after said  $^{225}\text{Ac}$  radioimmunoconjugate.

Claim 15 (original) The method of claim 13, wherein said chelator pentaacetic acid, calcium diethylenetriamine pentaacetic acid, or zinc diethylenetriamine pentaacetic acid.

Claim 16 (original) The method of claim 13, further comprising:  
administering a pharmacologically effective dose of a diuretic; and  
preventing accumulation of francium-211 daughters of said actinium-225 within the kidneys of the individual by inhibiting reabsorption of francium-211 therein with said diuretic thereby reducing nephrotoxicity during the radioimmunotherapeutic treatment.

Claim 17 (original) The method of claim 16, wherein said diuretic is administered prior to administering said  $^{225}\text{Ac}$  radioimmunoconjugate, said diuretic continuing to be administered after said  $^{225}\text{Ac}$  radioimmunoconjugate.

Claim 18 (original). The method of claim 16, wherein said diuretic is furosemide, chlorthiazide, hydrochlorothiazide, bumex, or other loop diuretic.

Claim 19 (original) The method of claim 13, wherein said  $^{225}\text{Ac}$  radioimmunoconjugate comprises an actinium-225 bifunctional chelant and a monoclonal antibody.

Claim 20 (original) The method of claim 19, wherein said  $^{225}\text{Ac}$  radioimmunoconjugate is [ $^{225}\text{Ac}$ ] DOTA-HuM195.

Claim 21 (original) The method of claim 13, wherein said pathophysiological condition is a cancer or an autoimmune disorder.

Claim 22 (original) The method of claim 21, wherein said cancer is a solid cancer, a disseminated cancer or a micrometastatic cancer.

Claim 23 (original) The method of claim 22, wherein said cancer is myeloid leukemia.

Claim 24 (original). A method of reducing nephrotoxicity in an individual during radioimmunotherapeutic treatment of a pathophysiological condition, comprising:

- administering a pharmacologically effective dose of a diuretic;
- administering an actinium-225 radioimmunoconjugate to treat the cancer; and
- preventing accumulation of francium-211 daughters of said actinium-225 within the kidneys of the individual by inhibiting reabsorption of francium-211 therein with said diuretic thereby reducing nephrotoxicity during the radioimmunotherapeutic treatment.

Claim 25 (original) The method of claim 24, wherein said diuretic is administered prior to administering said  $^{225}\text{Ac}$  radioimmunoconjugate, said diuretic continuing to be administered after said  $^{225}\text{Ac}$  radioimmunoconjugate.

Claim 26 (original) The method of claim 24, wherein said diuretic is furosemide, chlorthiazide, hydrochlorothiazide, bumex, or other loop diuretic.

Claim 27 (original) The method of claim 24, wherein said  $^{225}\text{Ac}$  radioimmunoconjugate comprises an actinium-225 bifunctional chelant and a monoclonal antibody.

Claim 28 (original) The method of claim 27, wherein said  $^{225}\text{Ac}$  radioimmunoconjugate is [ $^{225}\text{Ac}$ ] DOTA-HuM195.

Claim 29 (original) The method of claim 24, wherein said pathophysiological condition is a cancer or an autoimmune disorder.

Claim 30 (original) The method of claim 29, wherein said cancer is a solid cancer, a disseminated cancer or a micrometastatic cancer.

Claim 31 (original) The method of claim 30, wherein said cancer is myeloid leukemia.

Claim 32 (original) A method of improving radioimmunotherapeutic treatment of cancer in an individual, comprising:

- administering a pharmacologically effective dose of a chelator;
- administering an actinium-225 radioimmunoconjugate; and
- scavenging bismuth-213 daughters of the actinium-225 with said chelator to reduce nephrotoxicity in the individual during the treatment, thereby increasing the therapeutic index of the actinium-225 to improve the treatment for said cancer.

Claim 33 (original) The method of claim 32, wherein said chelator is administered prior to administering said  $^{225}\text{Ac}$  radioimmunoconjugate, said chelator continuing to be administered after said  $^{225}\text{Ac}$  radioimmunoconjugate.

Claim 34 (original) The method of claim 32, wherein said chelator is 2,3 dimercapto-1-propane sulfonic acid, meso 2,3-dimercapto succinic acid,

diethylenetriamine pentaacetic acid, calcium diethylenetriamine pentaacetic acid, or zinc diethylenetriamine pentaacetic acid.

Claim 35 (original) The method of claim 32, further comprising:  
administering a pharmacologically effective dose of a diuretic; and  
inhibiting renal uptake of francium-211 daughters of the actinium-225 with said diuretic to reduce nephrotoxicity in the individual during the treatment thereby increasing the therapeutic index of the actinium-225 to improve the treatment for said cancer.

Claim 36 (original) The method of claim 35, wherein said diuretic is administered prior to administering said  $^{225}\text{Ac}$  radioimmunoconjugate, said diuretic continuing to be administered after said  $^{225}\text{Ac}$  radioimmunoconjugate.

Claim 37 (original) The method of claim 35, wherein said diuretic is furosemide, chlorthiazide, hydrochlorothiazide, bumex, or other loop diuretic.

Claim 38 (original) The method of claim 35, wherein said  $^{225}\text{Ac}$  radioimmunoconjugate comprises an actinium-225 bifunctional chelant and a monoclonal antibody.

Claim 39 (original) The method of claim 38, wherein said  $^{225}\text{Ac}$  radioimmunoconjugate is [ $^{225}\text{Ac}$ ] DOTA-HuM195.

Claim 40 (original) The method of claim 35, wherein said cancer is a solid cancer, a disseminated cancer or a micrometastatic cancer.

Claim 41 (original). The method of claim 40, wherein said cancer is myeloid leukemia.

Claim 42 (original) A method of improving radioimmunotherapeutic treatment of cancer in an individual, comprising:

administering a pharmacologically effective dose of a diuretic;  
administering an actinium-225 radioimmunoconjugate; and  
inhibiting renal uptake of francium-211 daughters of the actinium-225 with said diuretic to reduce nephrotoxicity in the individual during the treatment thereby increasing the therapeutic index of the actinium-225 to improve the treatment for said cancer.

Claim 43 (original) The method of claim 42, wherein said diuretic is administered prior to administering said  $^{225}\text{Ac}$  radioimmunoconjugate, said diuretic continuing to be administered after said  $^{225}\text{Ac}$  radioimmunoconjugate.

Claim 44 (original) The method of claim 42, wherein said diuretic is furosemide, chlorthiazide, hydrochlorothiazide, bumex, or other loop diuretic.

Claim 45 (original). The method of claim 42, wherein said  $^{225}\text{Ac}$  radioimmunoconjugate comprises an actinium-225 bifunctional chelant and a monoclonal antibody.

Claim 46 (original) The method of claim 45, wherein said  $^{225}\text{Ac}$  radioimmunoconjugate is [ $^{225}\text{Ac}$ ] DOTA-HuM195.

Claim 47 (original) The method of claim 42, wherein said cancer is a solid cancer, a disseminated cancer or a micrometastatic cancer.

Claim 48 (original). The method of claim 47, wherein said cancer is myeloid leukemia.

Claim 49 (currently amended). A method of increasing the therapeutic index of an actinium-225 radioimmunoconjugate during treatment of a pathophysiological condition in an individual comprising:

inhibiting renal uptake of at least one alpha particle-emitting daughter of actinium-225 comprising; ~~by administering a pharmacologically effective amount of an adjuvant, wherein said adjuvant is a chelator, a diuretic, a competitive metal blocker, or a combination thereof effective for preventing accumulation of alpha-particle emitting daughters of Actinium-225~~ whereby nephrotoxicity is reduced during the treatment thereby increasing the therapeutic index of said actinium-225 radioimmunoconjugate.

Claim 50 (canceled) The method of claim 49, wherein inhibiting renal uptake of said <sup>225</sup>Ac daughter(s) comprises:

administering a pharmacologically effective amount of an adjuvant comprising:

- a chelator to scavenge said <sup>225</sup>Ac daughters therewith; or
- a diuretic to inhibit reabsorption of said <sup>225</sup>Ac daughters within a kidney; or
- a competitive metal blocker to prevent binding of said <sup>225</sup>Ac daughters within a kidney; or a combination thereof.

Claim 51 (currently amended) The method of claim 49 50, wherein said chelator and/or said diuretic and/or said competitive metal blocker are administered prior to treatment with said actinium-225 radioimmunoconjugate, said chelator and/or said diuretic continuing to be administered after said actinium-225 radioimmunoconjugate is administered to the individual.

Claim 52 (currently amended) The method of claim 49 50, wherein said chelator is 2,3 dimercapto-1-propane sulfonic acid, meso 2,3-dimercapto succinic acid, diethylenetriamine pentaacetic acid, calcium diethylenetriamine pentaacetic acid, or zinc diethylenetriamine pentaacetic acid.



Claim 53 (currently amended) The method of claim 49 ~~50~~, wherein said diuretic is furosemide, chlorthiazide, hydrochlorothiazide, bumex, or other loop diuretic.

Claim 54 (currently amended) The method of claim 49 ~~50~~, wherein said competitive metal blocker is bismuth subnitrate or bismuth subcitrate.

Claim 55 (currently amended I) The method of claim 49 ~~50~~, wherein said chelator scavenges the  $^{225}\text{Ac}$  daughter bismuth-213.

Claim 56 (currently amended ) The method of claim 49 ~~50~~, wherein said diuretic inhibits reabsorption of the  $^{225}\text{Ac}$  daughter francium-211.

Claim 57 (currently amended) The method of claim 49 ~~50~~, wherein said competitive metal binder prevents binding of the  $^{225}\text{Ac}$  daughter bismuth-213.

Claim 58 (original) The method of claim 49, wherein said actinium-225 radioimmunoconjugate is [ $^{225}\text{Ac}$ ] DOTA-HuM195.

Claim 59 (original) The method of claim 49, wherein said pathophysiological condition is a cancer or an autoimmune disorder.

Claim 60 (original) The method of claim 59, wherein said cancer is a solid cancer, a disseminated cancer or a micrometastatic cancer.

Claim 61 (original) The method of claim 60, wherein said cancer is myeloid leukemia.